

Application Serial No. 10/663,875
 Amplt. Dated May 15, 2006
 Reply to Notice to Comply dated April 19, 2006

Attorney Docket No. 89188.0050
 Customer No. 26021

Amendments to the Specification:

Please replace the paragraph beginning at page 7, line 15 with the following rewritten paragraph:

In an isolated RNA of the invention, the splice donor site may contain 5'-GU(A/-)GAG(G/U)-3', the splice acceptor site may contain 5'-G(A/U/-)(U/G)(C/G)C(U/C)(G/A)CAG-3' (SEQ ID NO: 1), a branch site may contain 5'-UACU(A/U)A(C/U)(-/C)-3', and a poly-pyrimidine tract may contain 5'-(U(C/U))₁₋₃(C/-)U₇₋₁₂C(C/-)-3' (SEQ ID NO: 2) or 5'-(UC)₇₋₁₂NCUAG(G/-)-3' (SEQ ID NO: 3). Functionally equivalents of these sequences (e.g., sequences containing modified nucleotides) are included in the invention. The intron RNA serves as or is further processed to become, e.g., an RNA encoding a polypeptide, or an antisense RNA, short-temporary RNA (stRNA), microRNA (miRNA), small-interfering RNA (siRNA), short-hairpin RNA (shRNA), long deoxyribonucleotide-containing RNA (D-RNA), or ribozyme RNA, each of which may be in either sense or antisense orientation. Design of antisense RNA, stRNA, miRNA, siRNA, shRNA, D-RNA and ribozyme RNA is well known in the art. The intron RNA region homologous or complementary to its target gene ranges from 14 to 2,000 nucleotides, most preferably between 19 and 500 nucleotides. The intron RNA may be 35-100% (i.e., any integral between and including 35 and 100) identical or complementary to its target gene. The preferred homology or complementarity is 35-65% and more preferably 41-49% for an shRNA, 40-100% and more preferably 90-100% for a sense or antisense RNA. The length of an siRNA/miRNA/shRNA may be 16-38 nucleotides, and preferably 19-25 nucleotides. Additionally, there may be one or more linker sequences, e.g., between the donor and the acceptor site and the antisense RNA, stRNA, siRNA, shRNA, D-RNA or ribozyme RNA sequence. The isolated RNA may further contain exons encoding a polypeptide for co-expression

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with the intron RNA. The polypeptide may be a normal protein, a missing protein, a dominant-negative protein, or a protein marker such as a fluorescent protein, luciferase, or lac-Z.